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Commentary

Graded motor imagery in the rehabilitation of children with Complex Regional Pain Syndrome (CRPS): Evidence still needed

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In recent times, a growing number of children with complex regional pain syndrome (CRPS) attending tertiary pain clinics across Australia report having used mirror therapies and laterality recognition tasks prescribed by their local therapists as part of a graded motor imagery (GMI) rehabilitation protocol.[1] GMI is a progressive motor imagery intervention with three key components applied successively. The intervention begins with a laterality recognition component, followed by imagined movements of the affected limb, and then mirror therapy exercises (Moseley, 2004a). This commentary will review the rationale for GMI and report on the current state of evidence for GMI interventions with children. Consideration will be given to what we can learn from the adult literature as well specific areas that require further pediatric research.

CRPS in children

CRPS is a chronic condition characterized by continuous, regional pain that is spontaneous or evoked (most commonly following a fracture) and is disproportionate in time and/or severity to the normal course of the known trauma or injury (Harden et al., 2013). The syndrome includes a combination of central sensitization of nociception, commonly with impaired balance of descending pain modulation systems, as well as a complex interaction with psychological or behavioral factors (Bruehl & Chung, 2006). Research has revealed that the primary and secondary somatosensory cortices (S1, S2) are directly linked to the pathophysiology of CRPS (Maihöfner et al., 2003). These cortices are shown to remodel in response to sensory input reforms related to CRPS (Gustin et el., 2012). Changes include imprecise localizations of tactile stimuli, changes in size and organization of the cortical map, changes in motor cortex representation and body perception disturbances with the degree of cortical reorganization being directly proportional with ongoing pain intensity, thus, making these areas targets for rehabilitation (Swart et al., 2009; Gustin et el., 2012). This holds promise given that children with CRPS have demonstrated considerable neural plasticity (Simons et al., 2014).

Various preinjury and postinjury factors may place some individuals at greater risk of the development of CRPS (for a review see Marinus et al., 2011; Bayle-Iniquez et al., 2015). CRPS may also develop in children but with significant differences in presentation (Lebel et al., 2008; Tan et al., 2008). In children, the neurological and/or sympathetic signs and symptoms appear less pronounced, with the lower limb more frequently affected (Tan et al., 2008). The syndrome appears more prevalent in girls, demonstrates cooler temperature (probably related to children's greater tendency to protection and disuse), changes in symptomatic areas with less edema, and occurs commonly following a minor injury (Low et al., 2007; Tan et al., 2008). Although CRPS expression differs in children and adults, it is considered the same clinical entity, with evidence suggesting identical pathophysiology (Maihöfner et al., 2003, Stanton-Hicks, 2010).

The development and rationale of GMI

The GMI program was developed for use with adults with CRPS to enhance the efficacy and feasibility of existing mirror therapy interventions (Moseley, 2004a,b, 2006). Mirror therapy typically involves the placement of the affected limb inside a mirror box such that the reflection of the unaffected limb replaces visual input from the affected limb. The intervention uses visual feedback to modulate somatic sensations by inhibiting pathologic somatic impulses through visual regulation (Ramachandran & Altschuler, 2009). It is thought that mirror therapy helps to reconcile sensory feedback to motor output.

There has been limited published work reporting on utilizing mirror therapy protocols with children, with the exception of three studies pertaining to children with spastic hemiparetic cerebral palsy (Feltham et al., 2010; Gygax et al., 2011; Smorenburg et al., 2011), one of which also included a control group of typically developing children (Feltham et al., 2010). The outcomes of interest in these studies (e.g. grasp strength, pinch strength, coordination tasks with both arms and neuromuscular activation) differ to those typically considered with CRPS patients. Nevertheless, these studies help establish the feasbility of using mirror therapy protocols with children (ranging in age from 6-17 years).

Although mirror therapy has been shown to be effective in the treatment of adults with CRPS in the acute stages, patients with more chronic CRPS have not responded well to mirror therapy (McCabe et al., 2003). McCabe et al. (2003) speculated that the poorer outcomes of mirror therapy with more chronic CRPS patients (i.e. lasting more than 1 year), may be due to one of two possible reasons. Firstly, with more chronic CRPS, the neural pathways are likely to be more established. Secondly, trophic changes, such as contractures, occur more commonly in chronic cases and may limit movement. In light of the limited efficacy of mirror therapy with patients beyond the acute stages of CRPS, Moseley (2004a) proposed two priming steps, namely laterality recognition tasks and imagined movement tasks, to facilitate the commencement of mirror therapy.

Laterality recognition tasks require patients to recognize pictures of a hand as either right or left; these being tasks which are presumed to require the mental rotation of the individual’s own hand. Laterality recognition activates areas of the brain associated with higher-order aspects of motor output (premotor cortices), but does not activate primary somatosensory and motor cortices (Ganis et al., 2000; de Lange et al., 2008; Cocksworth & Punt, 2013). Avoidance of early activation of motor cortices was considered important because movement execution commands are known to readily trigger pain responses (Melzack, 1990; Moseley, 2004a) in patients with conditions similar to CRPS (e.g. phantom limb pain). Moreover, laterality recognition tasks may be considered less threatening to patients than imagined movement or mirror therapy.

The second priming step in the GMI protocol involves more explicit motor imagery. Imagined motor tasks require individuals to imagine moving their affected limb to assume specific positions illustrated in various images. Evidence from numerous functional magnetic resonance imaging studies suggest that overlapping neural networks exist between explicit motor imagery tasks and physical movement, including the primary somatosensory and motor cortices (see Grèzes & Decety, 2001 for a meta-analysis). It has been postulated that explicit motor imagery can help activate neural pathways in preparation for movement (Moseley, 2005). However, the use of explicit imagery without a preliminary laterality task may result in increased pain and swelling in some adult patients with CRPS (Moseley, 2004b).

The GMI protocol has been proposed as an alternative to conventional management of adults with chronic CRPS, particularly for chronic CRPS-1 patients where conventional management has failed. Although the GMI protocol proposed by Moseley (2004a) suggests a definite sequence in which the tasks are to be administered, there is no evidence-based guidance regarding whether a certain degree of competence or practice is required before commencing the next step of therapy.

Efficacy of the 3-step GMI intervention

A systematic review evaluating the effects of GMI and its components on pain outcomes in adults with chronic pain resulted in the retrieval of six randomized controlled trials (Bowering et al., 2013). Only three of these trials evaluated the full GMI protocol (Moseley, 2004a, 2005, 2006) and were all carried out by the same research team. See Table 1 for a summary of the protocols used and key findings. The other three studies evaluated specific

Table 1
Overview of published GMI protocols, with sample specifics and key outcomes

Study: Moseley, 2004a
Sample: 26 adults with upper limb CRPS1
Laterality recognition tasks: 42 photographs of right hand taken in various postures and mirrored (84 images in total). Randomly selected 56 photographs. Patients required to identify whether left/right hand shown as quickly as possible. Response times and accuracy assessed. Patients were instructed to perform the task 3 times (~10 minutes) each waking hour.
Imagined movement tasks: 28 photos of the affected hand in various postures randomly selected from appropriate image bank. Patients were instructed to imagine assuming each posture 3 times (~15 minutes) each waking hour. Emphasis is on accuracy not speed.
Mirror movement tasks: 20 pictures from bank selected of unaffected hand involving less complicated postures. Patients were instructed to adopt each posture 10 times each waking hour.
Duration and sequence of tasks: 2 weeks each stage. Order of tasks: laterality recognition, imagined movements, mirror movements.
Key outcomes: Positive effect of treatment (relative to standard care control condition) on pain intensity and swelling, maintained for at least 6 weeks.

Study: Moseley, 2005
Sample: 20 adults with CRPS1 following a non-complicated wrist fracture > 6 months prior.
Laterality recognition tasks: 56 photographs of left and right hands randomly selected from a bank of 80 photographs. Patients were asked to identify whether left or right hand shown in images by clicking left/right mouse button. Response times and accuracy assessed. Patients instructed to perform the task 3 times (~10 minutes) each waking hour.
Imagined movement tasks: 28 photos of the affected hand selected and presented in random order. With affected hand resting comfortably, patients were asked to imagine assuming the posture in each picture. Advised to perform task twice (~10 minutes) every waking hour.
Mirror movement tasks: 20 pictures from bank selected of unaffected hand involving less complicated postures. Both hands places in a mirror box; affected hand concealed behind mirror. Instructed to adopt hand postures shown in each of the 20 images with both hands. Advised to perform task slowly and smoothly 5 times (~10 minutes) each waking hour.
Duration and sequence of tasks: 2 weeks each task. Order of tasks randomized.
Key outcomes: Laterality recognition resulted in minor reductions in pain intensity and disability. Imagined movements resulted in reductions in pain & disability but only if following laterality recognition. Mirror therapy task resulted in reduced pain and disability but only if it followed imagined movements.

Study: Moseley, 2006
Sample: 51 adults with phantom limb pain or CRPS1
Laterality recognition tasks: 40 photographs of a right hand, and 24 photographs of a right food (for each gender), in various positions and alignments, were digitally mirrored to create image banks of 80 hand images and 48 foot images for each gender. Patients indicated by pushing left or right button whether pictures showed a left or right limb. Response time and accuracy were assessed. Patients instructed to perform the task each waking hour.
Imagined movement tasks: Images of both limbs were randomly presented and subjects were advised to imagine twice adopting the posture shown with a smooth and pain-free movement. Patients were advised not to imagine watching themselves perform the movement but to imagine actually performing the movement. Patients instructed to perform the task each waking hour.
Mirror movement tasks: Patients were instructed to adopt each of the postures shown in the images twice, with both their hands in the mirror box, using smooth and pain-free movements. Patients instructed to perform the task each waking hour.
Duration and sequence of tasks: 2 weeks each task. Order: laterality recognition, imagined movement, mirror therapy.

Key outcomes: Image selection for each task manipulated to gradually increase task difficulty over 2 week period. Significant improvements in pain intensity and function in GMI treatment condition relative to standard care condition (with a comparable physiotherapy training load (i.e. hourly training).

Study: Johnson et al., 2012
Sample: 35 adult patients with CRPS type I or II from two centers commenced GMI protocol. (16 patients completed all three stages, i.e. completed the mirror task stage).
Laterality recognition tasks: Laterality recognition task was delivered using the commercially available, Recognise© program. Patients were shown how to create a personalized test which consisted of 30 images of either hands or feet depending on their presenting complaint. Patients advised to perform the test every waking hour. Response times and accuracy was recorded.
Imagined movement tasks: The Recognise© software was used for imagined movement task. Patients were advised to repeat the same test they had created for laterality training, but to increase the image display time to the maximum interval. Patients were instructed to imagine the movement required to adopt the posture shown in each consecutive image (skipping any they perceived as too hard) for approximately 10-15 minutes every waking hour. Emphasis was on accuracy not speed.
Mirror movement tasks: Patients were encouraged to watch the reflection of their unaffected hand in the mirror in order to create the illusion that the reflection was that of the affected hand. They then performed gentle movements for approximately 10 times, every waking hour. Patients were advised to stop if they had an increase in pain either during or directly after mirror therapy, and to keep a diary of training.
Duration and sequence of tasks: 2-4 weeks for each stage. Order: laterality recognition, imagined movement, mirror therapy. Some patients also received tactile discrimination task.
Key outcomes: No improvement in pain intensity with treatment. Patients in one centre, but not the other, reported functional improvement.

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components of the GMI protocol and were conducted by different teams (Chan et al., 2007; Cacchio et al., 2009; Michielsen et al., 2011). From the limited data available, Bowering et al. (2013) concluded that the 3-step sequential GMI intervention had moderate effects with respect to pain intensity relative to unordered GMI, and large effects when compared to usual physiotherapy (Bowering et al., 2013). Significant improvements in functioning were also reported for GMI relative to a conventional medical and physiotherapy control intervention (Moseley, 2006), with components necessarily in the prescribed order (Moseley, 2005) to achieve functional improvements. Notably, each of the six trials contained some inherent risk of bias, as determined using the Cochrane Collaboration's risk of bias tool (Bowering et al., 2013). Independent replication of the controlled GMI trials from the Moseley team remains a research priority. Subsequent to the search dates of the Bowering et al. (2013) review, another study evaluating the GMI protocol (also in collaboration with Moseley team), found contrary results (Johnson et al., 2012). The study involved 32 adult patients from two interdisciplinary centers and found that patients treated with a multimodal approach that included GMI were no better off than those who did not receive GMI. In fact, some patients treated with GMI reported increases in pain. Although these differences may have been due to unidentified baseline differences in the participant samples across the studies, differences in the study protocol should also be noted, specifically less face-to-face contact with a therapist and increased duration of the GMI which may have contributed to the poorer outcomes.

Application of GMI protocols with children who have CRPS

Given that there is no published work describing the application of adult GMI protocols for use with children, let alone any studies of the efficacy of this intervention with children, why are there seemingly growing numbers of therapists using GMI with children?

One wonders whether there is an erroneous perception amongst families, and perhaps even therapists, that although GMI is not of proven efficacy, there is no harm in trying. However, at least one adult study has found that some patients treated with GMI within a multimodal intervention were actually worse off than those who did not receive GMI (Johnson et al., 2012). Moreover, as seen with a motor imagery task alone (Moseley, 2004b), heightened pain may occur from such interventions.

It is not appropriate to assume that adult treatment protocols are necessarily appropriate for use with children. The cognitive developmental requirements of GMI are not well understood. Left-right confusion is common in young children (McManus et al., 1988), with left-right discrimination ability still developing below the age of 7 years (Belmont & Birch, 1963). About half of 11-year-olds are unable to accurately use the terms *left* and *right* with regard to other people (Rigal, 1994). Moreover, a study with school-aged children (not pain patients) found that the accuracy (but not the speed) of left-right judgments improved with age (Dey et al., 2012). Taken together, these studies suggest that younger children, perhaps under the age of about 11 years, may have difficulty doing laterality recognition tasks as part of a GMI protocol.

The cognitive developmental ability of children to generate motor imagery should also be considered. Although there is some evidence to suggest that this ability emerges by the age of about 7 years (Molina et al., 2008), another study found that 7- to 8-year-olds demonstrated reduced motor imagery ability relative to children aged 9 to 12 years (Caeyenberghs et al., 2009). Adults with chronic pain have been documented to have some reorganization in the primary sensory and motor homunculus (Henry et al., 2011); however, it is not known what changes may occur in children, within the context of a developing nervous system, and how these may impact on their motor imagery ability. A further limitation of this body of research is that although timed trials for motor imagery generation have been used with adults (Moseley, 2004a; Walz et al., 2013), and may prove useful with children, it is difficult to discern whether motor imagery is performed correctly or effectively (Osuagwu & Vuckovic, 2014). Thus, it is difficult to establish at what age GMI protocols can be implemented reliably with children.

Home practice is an important component of GMI protocols (Moseley, 2004a, 2006). However, adherence to home programs has been shown to be notoriously low for children and adolescents with chronic pain (Michaud et al., 1991), with this being attributed to factors such as patient-practitioner relations, parent or child forgetfulness, lack of time, parental perceptions of the condition, and a range of familial environmental factors (Michaud et al., 1991, Chappell & Williams, 2002). Importantly, reduced frequency of home practice of GMI may be associated with poorer pain outcomes in patients with CRPS (Johnson et al., 2012).

Further research

Given the known cortical reorganization associated with chronic pain (see Moseley & Flor, 2012 for a review), interventions that target cortical plasticity hold considerable appeal and potential in the context of chronic pain. Arguably, the greater cortical plasticity in the brain of a child suggests such interventions have much to recommend themselves and warrant further carefully designed investigation. However, even in adult pain populations, it is not yet clear how GMI interventions should be used alongside other physical therapies. Early physical therapies are widely recommended with CRPS patients (Howard, 2003; Wilder, 2006; Brooke & Janselewitz, 2012; Hoffart & Wallace, 2014), and more evidence is needed regarding whether a GMI intervention should occur prior to commencing physical therapies (thereby delaying the start of physical therapy), or whether physical therapies can be introduced during the GMI program. There may be a particular role for GMI interventions with patients who are to remain non-weight bearing due to fracture management but with concomitant CRPS symptoms, however, data is lacking. It is imperative that future studies present a variety of outcome measures, including pain intensity and measures of functional disability.

Prior to using GMI with children, it is important to establish age-appropriate protocols rather than applying protocols designed for adults. Randomized controlled trials can only be carried out once standardized protocols have been developed. To date, evaluations of GMI with adult pain patients have almost exclusively been carried out by the one research team, which limits the implications for generalizability, and heightens the potential for inherent biases.

Conclusions

Within the context of existing, moderately beneficial, non-invasive pediatric treatments for CRPS (Sherry et al., 1999; Lee et al., 2002; Wilder, 2006; Logan et al., 2012; Katholi et al., 2014), there is currently no evidence to support using GMI interventions with children in favor of multidisciplinary management and exercise therapy. Careful pediatric GMI protocol development is needed before clinical trials can be carried out to evaluate the efficacy of this treatment modality with children.

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End Notes

[1] This is consistent with the results of an informal survey of physiotherapists working in tertiary pediatric pain.

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